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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/521,393

07/21/2005

Mark W. Orme

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EXAMINER

MURRAY, JEFFREY H

ART UNIT

PAPER NUMBER

1624

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06/26/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/521,393	Applicant(s) ORME ET AL.	
	Examiner JEFFREY H. MURRAY	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 April 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) 1-22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 23 and 24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>8/4/2005</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. This action is in response to a restriction election filed on April 18, 2008. There are twenty-four claims pending and two claims under consideration. Claims 1-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant's election without traverse of Group III in the reply filed on April 18, 2008 is acknowledged. This is the first action on the merits. This invention relates generally to a modified Pictet-Spengler reaction for introducing a second stereogenic center into a compound. More particularly, the present invention relates to a modified Pictet-Spengler reaction that provides a desired *cis*- or *trans*-diastereomer of a polycyclic compound having two stereogenic centers, in high yield and high purity. This restriction is deemed proper and therefore made **FINAL**.

Priority

2. Acknowledgment is made of Applicant's claim for domestic priority. This application, U.S. Application No. 11/521,393, filed on July 21, 2005, is a national stage application of PCT/US03/322039, filed on July 14, 2003, which claims domestic priority to U.S. Provisional Application No. 60/400,386 filed on July 31, 2002 and U.S. Provisional Application No. 60/460,161 filed on April 3, 2003.

Specification

3. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any of the errors of which applicant may become aware of in the specification.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

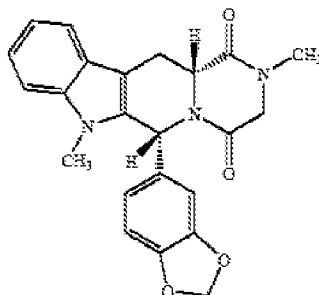
5. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Orme, et. al., U.S. Patent No. 7,098,209 (herein '209), in view of *In re Hass*, and *In re Henze*.

The present action relates to a modified Pictet-Spengler reaction for introducing a second stereogenic center into a compound.

Orme, et. al. teaches a method for preparing a compound having the following structure:



The compound shown above is prepared by the same procedure as claim 23 of the current application. This procedure, including all the limitations of steps a-d, can be seen in a diagram in column 13 and 14 of '209. The actual written procedure for these steps follows the diagram and are described in columns 14 and 15 of the reference. While the process to prepare this compound in '209 is identical to the process in the current application, there is one distinct difference. The current application describes a compound which lacks a methylated nitrogen on 5-membered heterocyclic ring, whereas the patent reference contains a methyl group on this nitrogen.

The CCPA has defined a homologous series as a family of chemically related compounds, the composition of which varies from member to member by a -CH₂ (one atom of carbon and two hydrogen). In re Coes, Jr. (CCPA 1949) 173 F2d 1012, 81 USPQ 369. The Court of Appeals for the District of Columbia applied a broader definition and defined a homolog (homologue) as a member of a series of compounds in which each member differs from the next member by a constant number of atoms. Carr. Pats.v. Deutsche Gold-und-Silber, etc. (CADC 1968) 397 F2d 656,157 USPQ 549.

The "Hass-Henze Doctrine" evolved from three CCPA cases, viz., *In re Hass et al.* (CCPA 1944) 141 F2d 122 and 127, 60 USPQ 544 and 548; and *In re Henze* (CCPA 1950) 181 F2d 198, 85 USPQ 261. In the *Henze* decision, the Court said:

"The nature of homologues and the close relationship the physical and chemical properties of one member of a series bears to adjacent members is such that a presumption of unpatentability arises against a claim directed to a composition of matter, the adjacent homologue of which is old in the art. The burden is on the applicant to rebut that presumption by a showing that the claimed compound possesses unobvious or unexpected beneficial properties not actually possessed by the prior art homologue. It is immaterial that the prior art homologue may not be recognized or known to be useful for the same purpose or to possess the same properties as the claimed compound. The CCPA concluded that because the characteristics normally possessed by members of a homologous series are principally the same, varying gradually from member to member, chemists knowing the properties of one member of a series would in general know what to expect in adjacent members so that a mere difference in degree is not the marked superiority which will ordinarily remove the unpatentability of adjacent homologues of old substances. Contra, where no use for the prior art compound is known. *In m Sterniski* (CCPA 1971) 444 F2d 581, 170 USPQ 343, and cases cited therein. Whether a compound is patentable over a prior art homologue or isomer is a question to be decided in each case. *In re Hass et al.*, *supra*."

The 'Hass-Henze Doctrine' stands for the proposition that, "If that which appears at first blush to be obvious though new is shown by evidence not to be obvious then the evidence prevails over surmise or unsupported contention and rejection based on obviousness must fail." *In re Papesch* (CCPA 1963) 315 F2d 381, 137 USPQ 43, 48. The presumption that homologues are unpatentably obvious is an inference of fact, viz., that adjacent homologs are expected to have similar properties which places a 'burden of persuasion' on the applicant who asserted a contrary fact. *In re Mills* (CCPA 1960) 281 F2d 218, 126 USPQ 513.

Here, there is nothing in the chemical arts to suggest that this methyl group is critical to the steps involved in the method of preparing the compound. Looking at the two compounds we see that the instantly claimed compound differs from the reference

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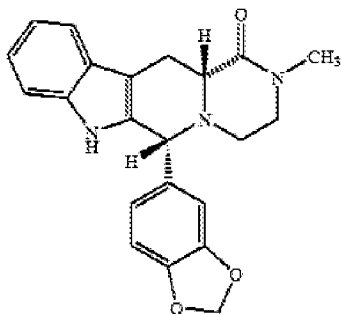
compound by only a -CH₂- group on the nitrogen. It would have been obvious to one having ordinary skill in the art at the time of the invention to attempt the method of the patent reference on a modified version of the compound in the prior art to prepare a structural homolog which corresponds to the compound of the current application. There is no teaching or suggestion that the methyl group located on the five-membered ring is critical to the method of preparing the final compound using the same procedure as the prior art.

One having ordinary skill in the art would have been motivated to prepare the instantly claimed compound using the same method because the methyl group is not critical to the synthesis of the final compound and such structurally homologous compounds are expected to possess similar properties. It has been held that compounds that are structurally homologous to prior art compounds are *prima facie* obvious, absent a showing of unexpected results. *In re Hass*, 60 USPQ 544 (CCPA 1944); *In re Henze*, 85 USPQ 261 (CCPA 1950).

7. Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Orme, et. al. U.S. Patent No. 6,878,711 (herein '711) in view of Orme, et. al., U.S. Patent No. 7,098,209 (herein '209). The present action relates to a modified Pictet-Spengler reaction for introducing a second stereogenic center into a compound.

Orme, et. al. teaches a method for preparing a compound having the following structure:

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The compound shown above is the identical compound of the current application and can be seen as “Example 1” in column 15 of the ‘711 patent reference. The procedure for the method of preparing this compound can be seen in column 15 and 16. The final step, or “step d” of this procedure is located in column 16, lines 5-34. Lines 1 and 2 state “A mixture of intermediate 1...and methylamine (6.0mL, 2.0M in THF, 12.0 mmol). This shows that the reaction was performed in THF. Lines 15 and 16 states, “The product was further purified by trituration with methanol (2mL).” This clearly shows that the THF solvent has been removed, and replaced with alcohol for the purposes of isolation and purification on the compound. Where this procedure differs from the current application is in steps a-c of the reference.

Steps a-c have already been shown to be obvious and well known in the art due to patent ‘209. Please see the arguments above in paragraph 6. Claim 24 differs only in the “step d” portion of claim 23.

One having ordinary skill in the art would have been motivated to prepare the instantly claimed compound using steps a-c of ‘209 in combination with step d of ‘711 to obtain the reference compound of the current application.

Conclusion

8. Claims 23 and 24 are rejected.
9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey H. Murray whose telephone number is (571) 272-9023. The examiner can normally be reached on Mon-Thurs. 7:30-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a US PTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey H Murray/
Patent Examiner
Art Unit 1624

James O. Wilson
Supervisory Patent Examiner, Art Unit 1624